

CLAIMS

1. A histamine or serotonin binding compound capable of binding to histamine or serotonin with a dissociation constant of less than $10^{-7}M$ and which has a binding site comprising amino acid residues phenylalanine, isoleucine or leucine at position I, tryptophan at position II and aspartate or glutamate at positions III and IV wherein residues I to IV are positioned substantially the same as residues 108, 42, 39 and 82 respectively in either of Figures 1 or 2, or residues 107, 41, 38 and 78 in Figure 3 or residues 122, 54, 50 and 95 in Figure 4, and functional equivalents thereof, wherein the numbering of the amino acid residues refers to the sequence of the mature protein that lacks the leader sequence.
2. A histamine or serotonin binding compound capable of binding to histamine or serotonin with a dissociation constant of less than $10^{-7}M$ and which has a binding site comprising amino acid residues phenylalanine or isoleucine at residue I, tryptophan at residue II and aspartate or glutamate at residues III and IV wherein residues I to IV are positioned substantially the same as residues 98, 137, 24 and 120 respectively in either of Figures 1 or 2, or residues 95, 138, 23 and 120 in Figure 3 or residues 112, 149, 35 and 135 in Figure 4, and functional equivalents thereof, wherein the numbering of the amino acid residues refers to the sequence of the mature protein that lacks the leader sequence.
3. A histamine binding compound capable of binding to histamine or serotonin with a dissociation constant of less than $10^{-7}M$ and which has two binding sites, the first binding site comprising amino acid residues phenylalanine, isoleucine or leucine at position I, tryptophan at position II and aspartate or glutamate at positions III and IV wherein residues I to IV are positioned substantially the same as residues 108, 42, 39 and 82 respectively in either of Figures 1 or 2, or residues 107, 41, 38 and 78 in Figure 3 or residues 122, 54, 50 and 95 in Figure 4, and the second binding site comprising amino acid residues phenylalanine or isoleucine at residue I, tryptophan at residue II and aspartate or glutamate at residues III and IV wherein residues I to IV are positioned substantially the same as residues 98, 137, 24 and 120 respectively in either of Figures 1 or 2, or residues 95, 138, 23 and 120 in Figure 3 or residues 112, 149, 35 and 135 in Figure 4, and functional equivalents thereof, wherein the

AMENDED SHEET

numbering of the amino acid residues refers to the sequence of the mature protein that lacks the leader sequence.

4. A histamine binding or serotonin binding compound according to claim 1 or 3 additionally comprising at residue V, a tyrosine residue, wherein residue V is positioned substantially the same as residue 100 in the sequence of either of Figures 1 or 2, residue 97 in Figure 3 or residue 114 in Figure 4, and functional equivalents thereof, wherein the numbering of the amino acid residues refers to the sequence of the mature protein that lacks the leader sequence.

5. A histamine or serotonin binding compound according to claim 2 or 3 additionally comprising at residue V, a tyrosine residue, wherein residue V is positioned substantially the same as residue 29 in the protein sequence of either of Figures 1 or 2, residue 28 in Figure 3 or residue 40 in Figure 4, and functional equivalents thereof, wherein the numbering of the amino acid residues refers to the sequence of the mature protein that lacks the leader sequence.

- a* 15. 6. A histamine or serotonin binding compound according to any preceding claim wherein said compound is stabilised by either or both of the disulphide bridges formed between cysteines 48 and 169 and cysteines 148 and 119 in the protein sequence of either of Figures 1 or 2, cysteines 47 and 175 and cysteines 151 and 119 of Figure 3 or cysteines 162 and 134 of Figure 4, wherein the numbering of the amino acid residues refers to the sequence of the mature protein that lacks the leader sequence.

- a* 7. A histamine or serotonin binding compound of any one of the preceding claims which comprises a peptide, or a fragment of any one of the proteins whose amino acid sequences are presented in Figures 1-4.

- 25 8. The histamine or serotonin binding compound of claim 7 that comprises a cyclic peptide.

9. The histamine or serotonin binding compound of claim 8 wherein said cyclic peptide comprises the sequence Ala-Glu-Ala-Phe-Ala-Glu-Ala-Trp.

203

10. The histamine or serotonin binding compound of any one of claims 1 to 9 that comprises a synthetic compound.

11. A protein comprising the Ra-Res amino acid sequence given in Figure 5 or functionally equivalent derivative or functionally equivalent fragment thereof.

5 12. A protein comprising the Av-HBP amino acid sequence given in Figure 6 or functionally equivalent derivative or functionally equivalent fragment thereof.

13. A protein comprising the Ih/Bm-HBP1 amino acid sequence given in Figure 7 or functional equivalent derivative or fragment thereof.

14. A protein comprising the Ih/Bm-HBP2 amino acid sequence given in Figure 8 or
10 functional equivalent derivative or fragment thereof.

15. A protein comprising the Ih/Bm-HBP3 amino acid sequence given in Figure 9 or functional equivalent derivative or fragment thereof.

16. A protein comprising the Ih/Bm-HBP4 amino acid sequence given in Figure 10 or functional equivalent derivative or fragment thereof.

15 17. A protein comprising the Ih/Bm-HBP5 amino acid sequence given in Figure 11 or functional equivalent derivative or fragment thereof.

18. The histamine or serotonin binding compound of any one of claims 1 to 10 or protein according to any one of claims 11 to 17 produced by recombinant DNA technology.

20 19. A histamine or serotonin binding compound or protein according to any one of the preceding claims that binds specifically to histamine.

Sub A >

20. The histamine or serotonin binding compound or protein of any one of the preceding claims having an effector or reporter molecule attached thereto.

21. The histamine or serotonin binding compound or protein of any preceding claim that is derived from blood-feeding ectoparasites, spiders, scorpions or snakes and venomous animals.

25 22. The histamine or serotonin binding compound or protein of claim 21 that is derived from ticks.

AMENDED SHEET

23. The histamine or serotonin binding compound or protein of claim 22 that is derived from Ixodid ticks.

24. The histamine or serotonin binding compound or protein of claim 23 that is derived from *Rhipicephalus appendiculatus*, *D. reticulatus*, *Amblyomma variegatum*,
5 *Boophilus microplus* or *Ixodes hexagonus*.

a 25. The histamine or serotonin binding compound or protein of any one of the preceding
1,2,3 or 5 claims associated with one or more carbohydrate moieties.

a 26. The histamine or serotonin binding compound or protein of any one of the preceding
1,2,3 or 5 claims that is associated with one or more peptides or polypeptides.

10 27. The histamine or serotonin binding compound or protein of claim 26 that is genetically or chemically fused to one or more peptides or polypeptides.

a 28. The histamine or serotonin binding compound or protein of any one of the preceding
1,2,3 or 5 claims attached to a label or toxin.

a 29. The histamine or serotonin binding compound or protein of any one of the preceding
1,2,3 or 5 claims that is bound to a support, such as a resin.
15

30. A therapeutic or diagnostic composition comprising a histamine or serotonin binding compound or protein according to any one of the preceding claims.
1,2,3 or 5

a 31. A therapeutic or diagnostic composition according to claim 30 additionally comprising serotonin.

20 32. A therapeutic or diagnostic composition according to claim 31 additionally comprising a cysteinyl leukotriene, platelet activating factor, or a thromboxane.

33. A vaccine comprising a histamine or serotonin binding compound according to any one of claims 1-10 or protein according to any one of claims 11-17.

34. The histamine or serotonin binding compound or protein according to any one of claims 1 to 29 or composition of any one of claims 30 to 32 for use in therapy.
25

AMENDED SHEET

35. The histamine or serotonin binding compound or protein according to any one of claims 1 to 29 for use as a pharmaceutical.

36. Use of the histamine or serotonin binding compound or protein according to any one of claims 1 to 29 as a pharmaceutical.

5 37. The histamine or serotonin binding compound or protein according to any one of claims 1 to 29 for use in a vaccine.

38. Use of the histamine or serotonin binding compound or protein according to any one of claims 1 to 29 in a vaccine.

a 39. The histamine or serotonin binding compound or protein of any one of claims 1 to 29 for use in the detection or quantification of histamine in human, animal, plant, and food material. ^{, 2, 3 (a) 5)}

a 40. The histamine or serotonin binding compound of any one of claims 1 to 29 for use in the depletion or removal of histamine from food products, cell cultures or human, animal, plant and food material. ^{, 2, 3 (a) 5)}

a 41. The histamine or serotonin binding compound of any one of claims 1 to 29 for use in the binding or detection of histamine in humans or animals. ^{, 2, 3 (a) 5)}

a 42. The histamine or serotonin binding compound or protein of any one of claims 1 to 29 for use as an anti-histamine agent, an anti-inflammatory drug or in the treatment of allergy. ^{, 2, 3 (a) 5)}

a 20 43. The histamine or serotonin binding compound or protein of any one of claims 1 to 29 for use as a tool in scientific research concerning the role of histamine in biological processes. ^{, 2, 3 (a) 5)}

44. The use of a histamine or serotonin binding compound according to any one of claims 1 to 29 in conjunction with a pharmaceutically-acceptable carrier in the manufacture of a medicament for the treatment or prevention of inflammation or allergic reaction in humans or animals.

45. A nucleic acid compound which encodes a histamine or serotonin binding molecule
or protein according to any one of claims 1-^{2, 3, or 5/}₁₀₋₂₉ or which hybridises with said
nucleic acid molecule under standard hybridisation conditions.

46. The nucleic acid molecule of claim 45 which comprises DNA, cDNA or RNA.

5 47. A cloning or expression vector comprising a nucleic acid molecule according to
^{Claim 45}
~~either of claims 45 or 46.~~

48. The vector of claim 47 which is virus based.

49. A host cell transformed or transfected with the vector of ~~either of claims 47 or 48.~~
^{Claim 47}

50. A transgenic animal that has been transformed by a nucleic acid molecule according
to either of claims 45 or 46 or vector according to either of claims 47 or 48.

Add a5

AMENDED SHEET